Fortifying cereal grains with folic acid not only prevented neural tube defects in about 1300 babies a year, but also "had a tremendous return on investment," noted Edward McCabe, MD, the March of Dimes chief medical officer. The FDA’s action has saved $400 million to $600 million annually on care for children who otherwise would have been born with spina bifida (http://1.usa.gov/1K0OurE3).

Hispanic Women at Risk
Even though fortifying cereals and grains has decreased the number of babies born with neural tube defects, CDC and March of Dimes experts said more work is needed to ensure that all women of childbearing age consume adequate folic acid by eating fortified foods and taking a daily supplement. Only 40% of women of childbearing age do so (CDC. MMWR Morb Mortal Wkly Rep. 2008;57[1]:5-8). The CDC and March of Dimes experts noted that adequate folic acid intake is particularly important for Hispanic women because they have a 21% higher risk of giving birth to a child with a neural tube defect than non-Hispanic white women (http://1.usa.gov/1S4pw3f). Crider explained that this may be partly due to Hispanic women being more likely to have a variant of the methylenetetrahydrofolate reductase (MTHFR) gene that results in reduced intracellular folate metabolism. In addition, they are less likely to consume recommended daily folic acid amounts: only 17% of Hispanic women report taking 400 μg or more of folic acid daily through fortified foods or supplements compared with 30% of non-Hispanic white women (Williams J et al. MMWR Morb Mortal Wkly Rep. 2015;64[1]:1-5).

Diet may play a large role. Hispanic adults tend to eat tortillas and other foods made with unfortified corn masa flour, rather than enriched cereal grain products, which is why the March of Dimes is lobbying for corn masa flour fortification, Crider noted. In 2012, the March of Dimes, American Academy of Pediatrics, National Council of La Raza, and Spina Bifida Association, along with 2 corn flour and food supplement manufacturers, petitioned the FDA to allow food manufacturers to voluntarily fortify corn masa flour with folic acid, said FDA spokesperson Megan McSeveney. At the FDA’s request, last October the March of Dimes submitted data on folic acid’s stability in corn masa flour, said Pellegrini. By April 15, the FDA will approve the request, deny it, or ask for additional information. Forty members of Congress sent a letter to the FDA in late February urging the agency to approve the request, Pellegrini said.

“The population with the highest risk hasn’t had the benefit of folic acid fortification,” McCabe said. “It would [have] a huge impact on the folic acid level in Hispanic women if we were able to fortify corn masa flour.”

The JAMA Forum

Cultural Influences Reflected in Divergent US vs UK Human Embryo Research Policies

Eli Y. Adashi, MD, MS

In a first, the Human Fertilisation and Embryology Authority (HFEA) of the United Kingdom recently approved a research application to use a gene-editing tool on early human embryos (http://nyti.ms/219K7DR). The applicant, Kathy K. Niakan, PhD, a developmental biologist with the Francis Crick Institute in London, England, is seeking to define the molecular program of the earliest stages of human development.

The studies would use surplus embryos from in vitro fertilization treatments donated by consenting parties and would conclude at the embryonic blastocyst stage without transfer to a recipient uterus. Preliminary experiments to edit out select genes with an eye toward delineating their role in cell lineage fate specification—how the single cell of an embryo develops into different cell lines—may soon be under way.

Although nonhuman embryo research has proceeded unabated on both sides of the Atlantic, nonhuman models may not be the answer. Insights derived using nonhuman models, critical in their own right, must be extrapolated with caution to the human context but cannot fully substitute for research performed on human embryos.

The dividends from human embryo research using genome editing could prove substantial. New insights into the relative inefficiency of human reproduction, the optimization of assisted...
conception, and the minimization of reproductive loss may emerge. Reactions to this latest milestone in the reproductive sciences, however, were mixed.

**Disparate Views**

Many UK scientists quoted in the lay and professional media welcomed the HFEA decision. Professor Sir Robert Lechler, MB, ChB, PhD, President of the UK Academy of Medical Sciences, offered that “studies such as [that proposed by Dr Niakan], that focus on asking basic questions about human-embryo development, are needed to help answer the many scientific and ethical questions remaining in this field” ([http://bit.ly/1RsfhkG](http://bit.ly/1RsfhkG)). Similar sentiments were echoed by other UK-based groups, including the Hinxton Group, an international consortium on stem cells, ethics, and law, the Wellcome Trust, an independent global charitable foundation dedicated to improving health, and the Medical Research Council, a leading funder of medical research ([http://bit.ly/1j9WT6A](http://bit.ly/1j9WT6A); [http://bit.ly/ITCzrgB](http://bit.ly/ITCzrgB); [http://bit.ly/ITb79ek](http://bit.ly/ITb79ek). Some prominent US scientists also spoke approvingly of such work going forward ([http://nyti.ms/219K7DR](http://nyti.ms/219K7DR)).

In contrast, some bioethics groups on both sides of the Atlantic criticized the HFEA’s action. Marcy Darnovsky, PhD, executive director of the Center for Genetics and Society, in Berkeley, California, warned that genome editing poses “dire safety and societal risks” ([http://apne.ws/1omYGI0](http://apne.ws/1omYGI0)). Calum MacKellar, PhD, of the Scottish Council on Human Bioethics, in Edinburgh, said that “allowing the gene editing of embryos opens the road to genetically modifying all the descendants of a person as well as full blown eugenics which was condemned by all civilised societies after the Second World War” ([http://bit.ly/1JTx9I3](http://bit.ly/1JTx9I3)).

Cultural fabrics play a key role in the formulation of science policy. A case in point is the divergent outlooks of the United Kingdom and the United States on human embryo research as informed by dissimilar positions across the prochoice/prolife divide. These distinctions are very much in evidence in the regulatory arena.

In the United Kingdom, human embryo research and public funding of it are allowed, subject to the issuance of a research license by the HFEA. However, editing of the genome of a human embryo followed by transfer to a recipient uterus is explicitly prohibited absent amendment of the Human Fertilisation and Embryology Act.

In the United States, which lacks an HFEA-like framework, human embryo research may proceed unencumbered at the discretion of local institutional review boards. Editing the genome of a human embryo absent intent to transfer remains similarly permissible subject to the discretion of local institutional biosafety committees. However, ventures beyond the laboratory into the clinic may not proceed without approval of the US Food and Drug Administration. Furthermore, the conduct of human embryo research in the United States remains ineligible for public funding due to statutory constraints.

**Frozen Funding**

This generation-long freeze in National Institutes of Health funding places the United States and US researchers at a competitive disadvantage. Dr. Niakan, for example, who was born, reared, and educated in the United States, now makes London’s Francis Crick Institute her scientific home.

It will take a major policy shift to restore US leadership in this arena. Until then, progress in the reproductive sciences in general, and in human embryo research in particular, is bound to largely remain the domain of a scientific universe an ocean away.

**Author Affiliation:**

Eli Y. Adashi, MD, MS, is a professor of Medical Science and the former dean of Medicine and Biological Sciences at the Warren Alpert Medical School of Brown University in Providence, Rhode Island.

**Corresponding Author:**

Eli Y. Adashi, MD, MS (Eli_Adashi@Brown.Edu).

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